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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,760	06/22/2000	Martha K. Newell	I0277/7009 HCL	8006

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/599,760	NEWELL, MARTHA K.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 9-30-05.

Claims 60-62 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claims 60-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons of record set forth in the Office action mailed 3-24-05.

Applicants' arguments filed 9-30-05 have been fully considered but they are not persuasive. Applicants argue that the instant invention is fully enabled for several reasons. Applicants argue that the instant specification has provided a description of lysosomal UCP inhibitors and their function, as well as a list of commercially available anti-UCP antibodies. Applicants also assert that lysosomal pH can be manipulated by manipulating lysosomal UCP expression and activity. If lysosomal UCP activity is inhibited by an antibody, Applicants assert, the lysosome can develop an acidic pH and potentially lead to both an increase in the promotion of antigen presentation by the cell and an increase in respiratory burst, in turn leading to an increase in the cell's ability to

treat intracellular pathogens. The examples and the specification, according to Applicants, adequately teach the regulation of lysosomal pH using anti-UCP antibodies.

Contrary to Applicants' assertions, the listing of known lysosomal UCP inhibitors and commercially available anti-UCP antibodies does not provide adequate teachings or the experimentation required for fully enabling the claimed invention. Furthermore, the commercially available antibodies listed in the instant specification are not identified as inhibitory antibodies, but are merely listed as antibodies that recognize UCP. The ability to bind UCP via Western blotting , ELISA or even in permeabilized cells using a commercially available antibody is not representative or correlative of the ability to administer an antibody to an intact cell in vitro or in vivo, wherein proper subcellular localization is achieved and inhibition of UCP activity is achieved by an antibody in the lysosome. The proper subcellular targeting and inhibition of molecular activity in a particular subcellular organelle requires undue experimentation beyond that taught in the instant disclosure. The cellular biology describing UCP's participation in the dissipation of protons in the lysosome, and the description of the potential role of UCP inhibition in enhancing a cell's immune defense system (*e.g.* by inhibiting UCP activity in the lysosome, thereby reducing the lysosomal pH and promoting respiratory burst, in turn potentially promoting antigen presentation by the cell and enhancing the cell's ability to treat intracellular pathogens, respectively) are neither representative nor correlative of the ability to successfully deliver sufficient quantities of intact, inhibitory antibodies to the proper subcellular location of target cells in vitro or in vivo, thereby inhibiting lysosomal UCP activity in that target cell.

Applicants also assert that it would take no more than routine experimentation to determine the ability of antibodies to bind to a lysosomal UCP using routine techniques such as Western blotting or an ELISA assay. Applicants also assert that the delivery of such antibodies has been achieved successfully using various methods. Contrary to Applicants' assertions, the detection of antibody binding using Westerns or ELISAs does not determine whether the antibody exhibiting binding to the target molecule is in fact inhibitory of that target molecule's activity. This requires experimentation beyond Westerns or ELISAs. And, once an inhibitory antibody has been identified, the delivery of it to the proper organelle, in sufficient concentrations and in proper conformation for binding and subsequent inhibition, requires undue experimentation beyond that provided in the art and in the instant disclosure. No teachings of intracellular inhibition of lysosomal UCP activity using inhibitory antibodies have been provided in the instant disclosure or in the art. Stayton stresses that intracellular delivery is a major challenge to achieving clinical efficacy: "Targeting to appropriate cells is not sufficient for therapy involving drugs which act intracellularly... The efficacy of several important protein and DNA therapeutics is subsequently limited by nonproductive intracellular trafficking..." (*see* Stayton, P. et al, J. Controlled Release, 65: 203-220, 2000, at p. 204, right column). Loboto also cautions that "Pre-formed antibodies injected into cells do facilitate functional interaction with antigen, but this approach is of limited valued for clinical applications" (*e.g.* requiring sufficient delivery, uptake and stability of intact antibodies). Alternatively, intrabody approaches are being developed, but are far from achieving routine clinical success: "A major challenge for the successful application of

intrabodies for therapy is achieving sufficient internalization or expression inside target cells." (*see* Lotobo et al, Trends in Molecular Med., 9(9): 390-396, 2003 at p. 392). Since the specification and art fail to provide sufficient guidance for the identification of anti-UCP antibodies that inhibit lysosomal UCP activity in a cell in vitro or in vivo, whereby the antibody is adequately delivered to the target cells and to the appropriate organelle, lysosomal UCP is appropriately modulated and lysosomal pH is appropriately regulated in vivo or in vitro, and since determination of the factors required to achieve this intracellular inhibition is highly unpredictable, the instant rejection for lacking enablement is maintained.

Rejections or Objections Necessitated by Amendments

Claim Objections

Claim 60 is objected to because of the following informalities: In claim 60, line 4, replacing "UCP antibody" with –anti-UCP antibody—would provide more clarity.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
11-16-05